Freeform Search

Database:
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- US Patents Full-Text Database
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Term:

Display: 10 **Documents in Display Format:** TI **Starting with Number** 1

Generate: ○ **Hit List** ◉ **Hit Count** ○ **Side by Side** ○ **Image**

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Search History

DATE: Wednesday, September 22, 2004 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT; PLUR=YES; OP=OR			
L6	l1 and nose	0	L6
L5	l1 and intranasal	0	L5
L4	l1 and mucosal	0	L4
L3	l1 and sublingual	0	L3
L2	L1 and pain	1	L2
L1	6261599.pn.	1	L1

END OF SEARCH HISTORY

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     CAPLUS, CEN, DISSABS, DGENE, DRUGB, DRUGMONOG2, IMSDRUGNEWS, DRUGU,
     EMBAL, EMBASE, ESBIOBASE, IFIPAT, IMSPRODUCT, IPA, JICST-EPLUS, KOSMET,
     LIFESCI, MEDICONF, MEDLINE, NAPRALERT, NLDB, ...' ENTERED AT 14:33:13 ON
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L1         6401 S TRAMADOL/TI
L2          133 S L1 AND (COMBINATION (P) OPIOID)
L3           56 DUP REM L2 (77 DUPLICATES REMOVED)
L4           27 S L3 AND PD<2003
L5            0 S L4 AND PROPOXYPHENE

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L6           24 S TRAMADOL (P) IMMEDIATE-RELEASE
L7            7 S L6 AND PROBLEM

     FILE 'STNGUIDE' ENTERED AT 14:50:10 ON 22 SEP 2004

     FILE 'USPATFULL' ENTERED AT 14:53:50 ON 22 SEP 2004
L8           63 S TRAMADOL/AB
L9            0 S L8 AND (IMMEDIATE-RELEASE (P) PROBLEM)
L10           0 S L8 AND (IMMEDIATE-RELEASE (P) DISADVANTAGE)
L11           0 S L8 AND ((IMMEDIATE (W) RELEASE) (P) DISADVANTAGE)
L12           0 S L8 AND ((IMMEDIATE (W) RELEASE) (P) PROBLEM)
L13          13 S L8 AND (IMMEDIATE (W) RELEASE)

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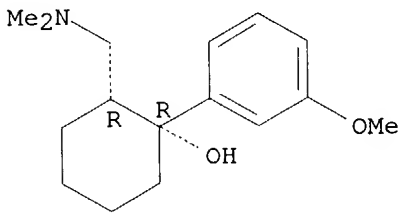
L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 27203-92-5 REGISTRY
CN Cyclohexanol, 2-[(dimethylamino)methyl]-1-(3-methoxyphenyl)-, (1R,2R)-rel- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Cyclohexanol, 2-[(dimethylamino)methyl]-1-(3-methoxyphenyl)-, cis-(±)-
CN Cyclohexanol, 2-[(dimethylamino)methyl]-1-(m-methoxyphenyl)- (8CI)
OTHER NAMES:
CN (±)-Tramadol
CN CG 315E
CN cis-Tramadol
CN E 265
CN Racemic tramadol
CN **Tramadol**
CN U 26255A
FS STEREOSEARCH
DR 113683-92-4, 73806-46-9
MF C16 H25 N O2
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, DDFU, DIOGENES, DRUGU, EMBASE, HSDB*, IMSCOSEARCH, IMSPATENTS, IPA, MEDLINE, MRCK*, PHAR, PROMT, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process); RACT (Reactant or reagent); USES (Uses)

Relative stereochemistry.

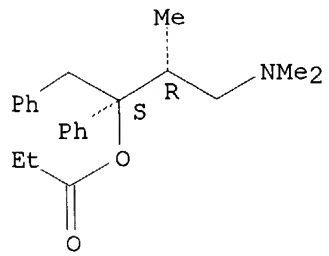


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

769 REFERENCES IN FILE CA (1907 TO DATE)
26 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
775 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 469-62-5 REGISTRY
CN Benzeneethanol, α-[(1R)-2-(dimethylamino)-1-methylethyl]-α-phenyl-, propanoate (ester), (αS)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2-Butanol, 4-(dimethylamino)-3-methyl-1,2-diphenyl-, propionate (ester), (2S,3R)- (8CI)
CN Benzeneethanol, α-[2-(dimethylamino)-1-methylethyl]-α-phenyl-, propanoate (ester), [S-(R*,S*)]-
OTHER NAMES:
CN (+)-4-(Dimethylamino)-3-methyl-1,2-diphenyl-2-butanol propionate
CN (+)-Propoxyphene
CN α-(+)-4-(Dimethylamino)-1,2-diphenyl-3-methyl-2-butanol propionate
CN α-d-4-(Dimethylamino)-3-methyl-1,2-diphenyl-2-(propionyloxy)butane
CN Algafan
CN d-Propoxyphene
CN Depromic
CN Dextropropoxyphene
CN **Propoxyphene**
FS STEREOSEARCH
DR 21086-94-2, 3818-94-8
MF C22 H29 N O2
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSPATENTS, IPA, MEDLINE, MRCK*, NIOSHTIC, PHAR, PIRA, PROMT, PS, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); MSC (Miscellaneous); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

928 REFERENCES IN FILE CA (1907 TO DATE)

26 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
933 REFERENCES IN FILE CAPLUS (1907 TO DATE)
3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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L6 ANSWER 1 OF 20 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

AB OBJECTIVES: To determine the medical conditions for which selected analgesics are most frequently prescribed in nursing facilities (NFs), describe the use of pharmacologic and nonpharmacologic pain therapies, and determine the frequency and quality of pain assessment in NF residents. DESIGN: A multicenter, 3-month retrospective drug use evaluation conducted by consultant pharmacists. SETTING: Eighty-nine NFs having no more than 25% of their patient census representing special populations (e.g., head trauma). PARTICIPANTS: A total of 2065 adult NF residents who received at least one selected analgesic. MEASUREMENTS: Primary indication for analgesics, pain type, method of pain assessment, nonpharmacologic therapies for pain, prescribed analgesics and regimens, and comorbid conditions were recorded. RESULTS: A total of 54.3% of residents had one indication for analgesic therapy, 31.0% had two indications, and 14.7% had three or more indications. Arthritis was the most prevalent indication for analgesics (41.7% of residents), followed by bone fracture (12.4%) and other musculoskeletal conditions (9.7%). More residents (76.8%) were reported to have chronic pain than acute pain (19.9%), and 3.0% had both chronic and acute pain. Pain type was unknown for 0.2% of residents. Observational pain assessments were used more frequently (for 55.9% of residents) than objective methods (16.6%), and pain was not assessed in 40.6% of residents. Most residents (69.4%) received no nonpharmacologic treatment for pain. Of the 2542 opioid and nonsteroidal anti-inflammatory drug (NSAID) prescriptions, 67.6% were for opioids, 24.8% were for NSAIDs, and 7.6% were for **tramadol**. **Propoxyphene**-containing drugs were the most frequently prescribed opioid group, and **propoxyphene** with acetaminophen was the most frequently prescribed analgesic (35.6% of all analgesics). Most analgesics (63.2%) were prescribed on an as-needed (prn) basis. CONCLUSIONS: The findings show a lack of adequate pain assessments, little use of nonpharmacologic interventions, and inappropriate use of analgesic medication. The small percentage of residents with chronic pain assessed objectively suggests the difficulty of monitoring pain progression in NFs. The prescribing of analgesic for most residents (with **propoxyphene** used most often, long-acting opioids used infrequently, and frequent prn use) was inconsistent with recommended pain therapy in older people and attests to the urgent need to educate NF practitioners on the appropriate use of analgesics.

L6 ANSWER 2 OF 20 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

AB Chronic pain affects 75 million US citizens. A number of pharmacologic treatments are available for chronic pain that does not respond adequately to nonpharmacologic methods. Long the mainstay of chronic pain management, nonsteroidal anti-inflammatory drugs (NSAIDs) are known to be associated with gastrointestinal (GI) and renal toxicities, a particular problem for the elderly population, which commonly experiences chronic pain, such as that associated with osteoarthritis (OA). Several non-NSAID, non-narcotic therapies are available for noninflammatory pain. Acetaminophen is as effective as NSAIDs for the management of mild-to-moderate OA pain and is the recommended first-line therapy by the American College of Rheumatology (ACR). **Propoxyphene**, widely believed to be safe and effective, may, in fact, be no more effective - and perhaps less effective-than acetaminophen or ibuprofen. A relatively new analgesic, **tramadol**, appears to be a useful therapy for patients who do not receive adequate pain relief with acetaminophen and are at risk for NSAID-related side effects. For localized chronic pain associated with OA, topical capsaicin is also an effective analgesic.

L6 ANSWER 3 OF 20 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

AB The analgesic effectiveness and safety of oral **tramadol** were compared with standard analgesics using a meta-analysis of individual patient data from randomised controlled trials in patients with moderate or severe pain after surgery or dental extraction. Calculation of %maxTOTPAR from individual patient data, and the use of gt 50%maxTOTPAR defined clinically acceptable pain relief. Number-needed-to-treat (NNT) for one patient to have gt 50%maxTOTPAR compared with placebo was used to examine the effectiveness of different single oral doses of **tramadol** and comparator drugs. Eighteen randomised, double-blind, parallel-group single-dose trials with 3453 patients using categorical pain relief scales allowed the calculation of %maxTOTPAR. The use of gt 50%maxTOTPAR was a sensitive measure to discriminate between analgesics. **Tramadol** and comparator drugs gave significantly more analgesia than placebo. In postsurgical pain **tramadol** 50, 100 and 150 mg had NNTs for gt 50%maxTOTPAR of 7.1 (95% confidence intervals 4.6-18), 4.8 (3.4-8.2) and 2.4 (2.0-3.1), comparable with aspirin 650 mg plus codeine 60 mg (NNT 3.6 (2.5-6.3)) and acetaminophen 650 mg plus **propoxyphene** 100 mg (NNT 4.0 (3.0-5.7)). With the same dose of drug postsurgical patients had more pain relief than those having dental surgery. **Tramadol** showed a dose-response for analgesia in both postsurgical and dental pain patients. With the same dose of drug postsurgical pain patients had fewer adverse events than those having dental surgery. Adverse events (headache, nausea, vomiting, dizziness, somnolence) with **tramadol** 50 mg and 100 mg had a similar incidence to comparator drugs. There was a dose response with **tramadol**, tending towards higher incidences at higher doses. Single-patient meta-analysis using more than half pain relief provides a sensitive description of the analgesic properties of a drug, and NNT calculations allow comparisons to be made with standard analgesics. Absolute ranking of analgesic performance should be done separately for postsurgical and dental pain.

L6 ANSWER 4 OF 20 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

AB To date in the United States when a patient has presented with a complaint of pain requiring some form of pharmacologic relief, the physician has had the choice of two broad classes of drugs: peripherally acting (i.e., NSAID) or centrally acting (i.e., opioid) analgesics. The antidepressant monoamine reuptake inhibitors, particularly when combined with an opioid analgesic, have also proven efficacious in treating certain types of pain conditions. A new approach, available for almost 20 years in Europe and recently approved for use in the United States, is the centrally acting synthetic analgesic **tramadol** HCl. Preclinical evidence suggests that **tramadol** produces its antinociceptive effect in animals and analgesic effect in humans through a complementary dual mechanism of action. One mechanism relates to its weak affinity for mu-opioid receptors (6,000-fold less than morphine, 100-fold less than d-**propoxyphene**, 10-fold less than codeine, and equivalent to dextromethorphan). A metabolite (O-desmethyltramadol; M1) binds to opioid receptors with a greater affinity than the parent compound and could contribute to this component. However in most animal tests and human clinical trials, the analgesic effect of **tramadol** is only partially blocked by the opioid antagonist naloxone, suggesting an important nonopioid mechanism. This nonopioid mechanism possibly relates to an increase in central neuronal synaptic levels of two neurotransmitters, 5-hydroxytryptamine (5-HT; serotonin) and norepinephrine. The opioid and nonopioid mechanisms appear to combine in a supra-additive manner in several tests of antinociception, but only in an additive or even counteracting manner in measures of adverse-effect liability. In sum, the apparent dual mechanism of action of

tramadol suggests a possible new approach to pain relief.

L6 ANSWER 5 OF 20 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

AB Although it is well established that the analgesic effects of morphine are mediated by opioid receptors, previous studies have shown that some opioids additionally inhibit the uptake of serotonin and norepinephrine. The present investigation of a diverse group of opioids revealed that structurally identifiable subgroups inhibited the neuronal reuptake of these monoamines. Phenanthrene opioids with an oxygen bridge between C4 and C5, such as morphine and naloxone (group I), did not block norepinephrine or serotonin uptake, whereas phenanthrene opioids without the oxygen bridge and the C6-OH moiety, such as levorphanol and levomethorphan (group II), did inhibit uptake, as did nonphenanthrene opioids, such as d-**propoxyphene** and methadone (group III). Affinity at the mu opioid receptor correlated with antinociceptive potency (r = 0.87, P lt .05). Although the antinociceptive activity of the "active enantiomers" of group II and III compounds also correlated with their affinity at the mu opioid receptor (r = 0.85, P = .007), additional consideration of serotonin uptake inhibiting activity (but not of norepinephrine uptake inhibiting activity) significantly improved the correlation between antinociceptive potency and the in vitro activity of these compounds (r = 0.915, P = .0017). Additionally, for group II and III (but not group I) compounds, smaller differences between enantiomers in antinociceptive potency than in mu receptor affinity were noted, presumably because of the contribution of uptake inhibition to the antinociceptive activity of group II and III compounds. Evidence also is provided suggesting a broader role for the combination of mu opioid affinity and 5-hydroxytryptamine uptake inhibition in the activity of other antinociceptive agents.

L6 ANSWER 6 OF 20 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

AB **Tramadol** hydrochloride is a synthetic opiate agonist with a plasma elimination half-life of 5 to 6 hours and peak plasma levels at about 1 1/2 hours. It derives its activity from attachment to the μ-receptor and blockage of norepinephrine reuptake. The purpose of this single-dose, double-blind, placebo-controlled study was to determine the analgesic effectivness of an oral administration of two dose levels of **tramadol** hydrochloride (75 or 150 mg) compared with the combination of 650 mg acetaminophen plus 100 my **propoxyphene** napsylate in 161 patients with severe postoperative pain after cesarean section. Analgesia was assessed over a 6-hour period. Treatments were compared on the basis of standard scales for pain intensity and relief and a number of derived variables based on these data. A global rating of the study medication was also used to compare treatments. The three active treatments were effective analgesics, statistically superior to placebo for many hourly and summary measures. A dose response was seen between the two **tramadol** doses, with the 150 mg dose providing significantly greater analgesia over the lower dose. The 75 mg dose of **tramadol** was generally more effective than the acetaminophen-propoxyphenic combination after hour 2, and significantly so for some hourly time points, as well as for the globual rating of the medication. The 150 mg dose of **tramadol** was significantly more effective than the acetaminophene-**propoxyphene** combination from hour 2 through hour 6 for the sum of pain intensity differences and total pain relief scores, as well as for the global rating of the medication. **Tramadol** hydrochloride at both dose levels is an effective analgesic agent and at 150 mg is statistically superior to the acetaminophen-**propoxyphene** combination. No serious adverse effects were observed; however, dizziness was more frequently reported with 150 mg **tramadol**.

L6 ANSWER 7 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
AB Four postmortem cases are reported in which the analgesic drug **tramadol** was identified. **Tramadol** is an alkaline extractable drug and elutes from a HP-5 column without the need for derivatization. Two metabolites of **tramadol**, N-desmethyl and O-desmethyl **tramadol** were also identified. Heart blood concns. of **tramadol** in the four cases ranged from 0.17 to 4.4 mg/l. Tissue distribution of **tramadol** in the four cases failed to identify a sequestration site. None of the deaths reported were attributed to **tramadol** intoxication.

L6 ANSWER 8 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
AB A review with .apprx.33 refs. To date in the United States when a patient has presented with a complaint of pain requiring some form of pharmacol. relief, the physician has had the choice of two broad classes of drugs: peripherally acting (i.e., NSAID) or centrally acting (i.e., opioid) analgesics. The antidepressant monoamine reuptake inhibitors, particularly when combined with an opioid analgesic, have also proven efficacious in treating certain types of pain conditions. A new approach, available for almost 20 yr in Europe and recently approved for use in the United States, is the centrally acting synthetic analgesic **tramadol** HCl. Preclin. evidence suggests that **tramadol** produces its antinociceptive effect in animals and analgesic effect in humans through a complementary dual mechanism of action. One mechanism relates to its weak affinity for μ-opioid receptors (6000-fold less than morphine, 100-fold less than d-**propoxyphene**, 10-fold less than codeine, and equivalent to dextromethorphan). A metabolite (O-desmethyltramadol; M1) binds to opioid receptors with a greater affinity than the parent compound and could contribute to this component. However, in most animal tests and human clin. trials, the analgesic effect of **tramadol** is only partially blocked by the opioid antagonist naloxone, suggesting an important nonopioid mechanism. This nonopioid mechanism possibly relates to an increase in central neuronal synaptic levels of two neurotransmitters, 5-hydroxytryptamine (5-HT; serotonin) and norepinephrine. The opioid and nonopioid mechanisms appear to combine in a supra-additive manner in several tests of antinociception, but only in an additive or even counteracting manner in measures of adverse-effect liability. In sum, the apparent dual mechanism of action of **tramadol** suggests a possible new approach to pain relief.

L6 ANSWER 9 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
AB Characteristics of withdrawal signs of several opioids were compared in rats after short-term frequent i.v. infusions. Male Sprague-Dawley rats with catheters implanted in the jugular veins were infused with a fixed dose of a drug hourly for 72 h. Thirty min after the final infusion, naloxone 4 mg/kg, s.c. was administered and withdrawal signs were observed for 1 h and the severity of the withdrawal signs was scored, classified into a behavioral sign score, autonomic sign score, and body weight loss score. As a result, total withdrawal scores of morphine, methadone, d-**propoxyphene**, loperamide, **tramadol**, and pentazocine were significantly higher than that of saline, with the highest score being observed for 4 mg/kg or more of morphine. The total score of ethylketocyclazocine was slightly but significantly higher than that of saline. Buprenorphine and thebaine produced no observable withdrawal signs. The behavioral sign score tended to be higher than the other 2 scores in the drugs showing relatively low but significant total scores such as **tramadol**, pentazocine, and ethylketocyclazocine, while the score of autonomic signs or the body weight loss tended to be higher in drugs showing high total scores. Thus, in the case of opioids, it is considered that the severity of withdrawal signs was mainly derived from the autonomic signs including diarrhea which may result in body weight loss.

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AB An analysis of the treatment of nonmalignant pain in the elderly at a long-term facility was conducted to allow development of a pain management program that complies with both JCAHO guidelines for pain management and with the Tennessee Medicaid (TennCare) reimbursement schedule, and to determine if **tramadol** can meet the standards of pain management under these new guidelines. Inclusion criteria were residence in our long-term care facility; a pain intensity score > 4 on a modified Wong Baker Pain Scale; the patient having prescription orders for one or more of the following drugs: **propoxyphene**, meperidine, or high dosages of acetaminophen (approaching 4 g/day); suspected neuropathic or mixed nociceptive/neuropathic pain; and/or a diagnosis of diabetes, osteoarthritis, or degenerative joint disease. Exclusion criteria were history of seizures, history of opioid or alcohol abuse, and demonstrated hypersensitivity to **tramadol** or opioids. **Tramadol** administration began at a dose of 25 mg/day titrated up to a maximum of 300 mg/day over a 16-day period. Data were collected from computer records, dispensing reports, medication administration reports (MARs), current federal minimum data set (MDS) data, and weekly care plan meetings. Data were tabulated at baseline and 4-6 weeks after a stable dose of **tramadol** had been established. Fourteen residents (mean age 85 years, 1 male, 13 female) met the criteria and received **tramadol** up to 300 mg/day (qid). **Tramadol** reduced the residents' pain scores from an average of 6 to 2 using the Modified Wong Baker Pain Scale, reduced the percentage of residents taking **propoxyphene** from 50% to 14%, and reduced those taking high doses of APAP or APAP products from 43% to 14%. **Tramadol** reduced the percentage of residents falling, losing weight, showing no change or decline in activities in daily living (ADLs), displaying inappropriate behavioral symptoms, suffering depression, and/or taking psychotropic medications. In the state of Tennessee, new reimbursement schedules by TennCare have allowed our hospital to comply with the JCAHO standards of "optimal achievable care" for the treatment of pain by allowing the hospital staff to treat patients with newer, safer, more effective analgesics such as **tramadol**. Early results from this ongoing study have shown that **tramadol** can provide a safe and effective treatment on nonmalignant pain in a long-term care facility and improve adherence to JCAHO and TennCare standards for proper pain management.

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AB In patients with renal or hepatic failure, the pharmacokinetics of opioids may be affected in several ways, leading to the necessity to correct the dose. The liver is the major site for biotransformation of most opioids. The major metabolic pathway is oxidation. Exceptions to this are morphine and buprenorphine, which undergo primarily glucuronidation, and remifentanil which is cleared by esther hydrolysis. The hydrophilic metabolites are predominantly excreted by the kidneys and may accumulate in patients with renal insufficiency. Some metabolites such as morphine-6-glucuronide (M6G) or normeperidine are active opioid agonists. With high concentrations they may cause narcotic effects or respiratory depression. In addition, special risks are known for normepridine that has been shown to exert neurotoxic effects with the risk of seizures. Few cases of respiratory depression following the administration of codeine, dihydrocodeine and tramdol have been reported. The elimination half-life of these drugs was prolonged. Lastly, the disposition of methadone, buprenorphine, fentanyl, sufentanyl and remifentanil appears to be unaffected in renal failure. In patients with hepatic cirrhosis it has been shown that oxidation of opioids is reduced, resulting in a decreased

drug clearance (meperidine, **propoxyphene**, pentazocine, **tramadol** and alfentanil) and increased oral bioavailability due to reduced first-pass metabolism (meperidine, **propoxyphene**, pentazocine, dihydrocodeine). Although glucuronidation is thought to be less affected in liver cirrhosis, the clearance of morphine was found to be decreased and its oral bioavailability increased. The consequence of reduced drug metabolism is the risk of accumulation in the body, especially with repeated administrations. As for patients with renal failure, special risks are known for meperidine with potential accumulation of normeperidine, which can cause seizures, and for **propoxyphene** for which several cases of hepatotoxicity have been reported. On the other hand, the analgesic activity of codeine and tilidine depends on transformation into the active metabolites, morphine and nortilidine. In the case of reduced metabolism in chronic liver disease, the analgesic action of these drugs may be compromised. Lastly, the disposition of a few opioids, such as fentanyl, sufentanil, and remifentanil, appears to be unaffected in liver disease.

L6 ANSWER 12 OF 20 EMBASE
on STN

AB Opioid analgesics are among the most commonly prescribed medications. Frequently, they are combined with other therapeutic agents and pharmacodynamic or pharmacokinetic interactions may ensue. This review summarizes published case reports and studies of potential opioid drug interactions. A MEDLINE computer literature search (1966-1998) was undertaken to retrieve all pertinent case reports and studies of opioid drug interactions published in the English language. The results of the search indicate that numerous compounds from various therapeutic classes may participate in clinically significant pharmacodynamic and pharmacokinetic drug-drug interactions. Pharmacodynamic interactions usually involved additive central nervous system depression. Additionally, **propoxyphene** and **tramadol** can potentiate a hyperserotonergic state when coadministered with the SSRIs and MAOIs. Pharmacokinetic interactions typically involved inhibition or induction by specific hepatic cytochrome P-450 isoenzymes. Agents with enzyme inhibiting ability such as erythromycin, cimetidine, and selective serotonin reuptake inhibitors have been shown to potentiate the effects of certain opioid analgesics while codeine, which requires metabolic conversion via CYP 2D6 for pharmacological effectiveness, has reduced analgesic efficacy in the presence of inhibitors. The enzyme inducers rifampin and several anticonvulsants have been involved in the emergence of methadone withdrawal when added to existing methadone treatment. Additionally, enzyme inducers can increase the formation of the toxic metabolite of meperidine. Genetic polymorphism also potentially impacts the effectiveness of agents such as codeine since reduced active metabolite formation and analgesic efficacy has been demonstrated in individuals who lack CYP 2D6 activity.

L6 ANSWER 13 OF 20 TOXCENTER on STN

AB The epidemiology and treatment strategies for opiate and opioid abuse and poisonings have continually evolved. Diversion of and accidental deaths from these agents have been a national public health concern and tempered their use in pain management. This presentation utilizes illustrative cases to highlight new trends in abuse, toxicological mechanisms and pathophysiology, signs and symptoms, use of the laboratory, and management strategies for opiate and opioid poisonings. Licit and illicit substances will be profiled and include: heroin, oxycodone, dextromethorphan, fentanyl, **tramadol**, **propoxyphene**, meperidine, heroin substitutes, designer drugs, and adulterants. Learning objectives: 1. Characterize and contrast the toxicology and management strategies for the prototypical opiates and opioids. 2. Recognize risk factors for opiate and opioid poisoning deaths. 3. Describe the recent abuse trends for

dextromethorphan, illicit and prescription agents. Self-assessment questions: Multiple-choice: 1. Which of the following agents is associated with wide-complex cardiac arrhythmias not responsive to naloxone? A. Heroin B. Fentanyl C. Oxycodone D. **Propoxyphene** E. Meperidine 2. Which of the following would be considered a risk factor for an opiate or opioid poisoning death? A. Tolerance to the loss of hypercarbic respiratory drive B. Ingestion by young children C. External stimulus applied to an intoxicated patient D. Use of high dose naloxone E. History of withdrawal 3. Which of the following is correct about the abuse and toxicology of dextromethorphan? A. Lack of CYP 2D6 may lead to more intense psychotomimetic effects. B. It is commonly administered by insufflation of crushed tablets. C. Naloxone will reverse all CNS effects. D. Miosis and respiratory depression are common signs and symptoms E. It may cause a false positive urine screen for phencyclidine. <A-B> Answers: 1.(D); 2.(B); 3.(E).

L6 ANSWER 14 OF 20 TOXCENTER COPYRIGHT 2004 ACS on STN

AB The 22nd French pharmacovigilance meeting, held in July 2001, presented data on adverse effects notified by health professionals to regional pharmacovigilance centres in France. Non specific "immunostimulants" are not harmless placebos, as might be concluded from the relative lack of data. There have been 315 notifications of severe adverse effects, some with positive rechallenge, reporting cutaneous, gastrointestinal, respiratory, haematological and other disorders. Attributability was considered likely in 68% of cases. Three deaths occurred. Other well known adverse effects continue to occur: convulsions with camphor, visual hallucinations with oxybutynin, headache with antimigraine drugs, liver damage with dextropropoxyphene, neuropsychological disorders after buflomedil overdose (especially in patients with renal failure), hyperkalaemia during spironolactone combination with an angiotensin-converting-enzyme inhibitor (ACE inhibitor), and severe infections after intravesical BCG. Rare adverse effects of old drugs were identified, such as oedema with valproic acid, interstitial pneumonia with flecainide, and a bleeding risk due to **tramadol** interaction with oral anticoagulants. The adverse effects of new drugs are better documented: celecoxib is now implicated in visual disorders. Overall, the meeting confirmed that only a small proportion of adverse drug reactions are notified, that a large number of hospitalised patients suffer from drug induced complications, and that summaries of product characteristics (SPC) are often too brief or reassuring regarding pharmacovigilance data. The poor risk-benefit ratios of some drugs call for their immediate market withdrawal.

L6 ANSWER 15 OF 20 TOXCENTER COPYRIGHT 2004 ACS on STN

AB Auditory hallucinations attributed to 50 mg of **tramadol** hydrochloride given 4 times daily for terminal cancer pain is reported in a 74 yr old male patient with lung cancer. Changing the therapy from **tramadol** to co-proxamol, a combination of 32.5 mg of **propoxyphene** hydrochloride (dextropropoxyphene hydrochloride) and 325 mg of acetaminophen (paracetamol), 4 times daily controlled the patient's pain and led to resolution of the hallucinations within 2 days. It was noted that this is the first report of this side effect. Peggy L. Ruppel

L6 ANSWER 16 OF 20 TOXCENTER COPYRIGHT 2004 ACS on STN

AB OBJECTIVE: Heroin is mainly abused drug in China. However, the pattern of polydrug abuse is increasing among heroin addicts in recent years. METHODS: In order to survey polydrug abuse, an epidemiol. study was carried out among 657 drug addicts from 6 different areas of Beijing, Guizhou, Xian, Haerbin, Wuhan and Yunnan by using a self-designed questionnaire. RESULTS: The results showed that 90.3%(593/657) of

subjects had the history of polydrug abuse. With the exception of illegal drugs of heroin and opium, the majority of abused drugs were controlled medical narcotics and psychotropic drugs such as pethidine, buprenorphine, triazolam and diazepam. The five most abused drugs were triazolam (425 cases), diazepam (401 cases), **tramadol** (327 cases), DHE (253 cases) and pethidine (243 cases), and most drug addicts could get those above five drugs easily from illogical routes. The main source of narcotic drugs was from black market, and the psychotropic drugs was from private drug store. CONCLUSION: The reasons of polydrug abuse among drug abusers were complex and multifactorial. First, drug addicts tried to substitute heroin temporarily with other narcotics or psychotropic drugs; furthermore, they tried to treat "protracted withdrawal syndrome" after acute detoxification; finally, some drug addicts want to seek particular psychol. effects from polydrug abuse, on specially, produced by interaction of different drugs. This results suggested that it is necessary to strength on the drug administration and to prevent diversion of narcotic and psychotropic drugs.

L6 ANSWER 17 OF 20 TOXCENTER COPYRIGHT 2004 ACS on STN
AB An overview of the use of opioids, including morphine, methadone, levorphanol tartrate (Levo-Dromoran), fentanyl, **tramadol** hydrochloride (Ultram), and **propoxyphene**, in the treatment of chronic, nonmalignant pain is presented, and definitions of physical dependency, tolerance, addiction, abuse, and pseudoaddiction in the context of opioid therapy for pain, the management of pain, the adverse effects of opioids, treatment regimens with these agents, and pharmacists' concerns about opioids are considered; a table listing equianalgesic doses of opioid analgesics is provided.
Ramune T. Dailide

L6 ANSWER 18 OF 20 TOXCENTER COPYRIGHT 2004 ACS on STN
AB The clinical assessment file on **tramadol** is of low quality. In acute postoperative pain and chronic pain there is no proof that **tramadol** has a better risk-benefit ratio than the paracetamol + codeine combination or other step 2 analgesics in the World Health Organisation classification. Like all other central analgesics, **tramadol** can have neuropsychological adverse effects, especially a risk of dependence and misuse.

L6 ANSWER 19 OF 20 TOXCENTER COPYRIGHT 2004 ACS on STN
AB A randomized, double-blind, multicenter study comparing the effectiveness of **tramadol** hydrochloride with that of **propoxyphene** napsylate (dextropropoxyphene napsylate) was conducted in 264 patients (ages 32-87 yr) with pain due to osteoarthritis who received an oral capsule of 100 mg **tramadol** or **propoxyphene** 3 times daily for 2 wk. At the end of the second wk, 71.6 and 70.4% of **tramadol** patients and 53.2 and 50.5% of **propoxyphene** patients had symptom improvement during daily activities and on walking, respectively. Improvement of pain during sleep was reported by 44.3% of **tramadol** patients and 30.3% of **propoxyphene** patients.
No potentially serious side effects were reported. **Tramadol** was associated with a significantly higher number of adverse events. It was concluded that **tramadol** is more effective than **propoxyphene** in treating osteoarthritic pain, but is more often associated with adverse effects.
Ellen Katz Neumann

L6 ANSWER 20 OF 20 TOXCENTER COPYRIGHT 2004 ACS on STN
AB The purpose of this single-dose, double-blind, placebo-controlled study was to determine the analgesic efficacy over a 6 h period of an oral administration of 2 dose levels of **tramadol** hydrochloride (75 or 150 mg) compared with the combination of 650 mg acetaminophen plus 100 mg

propoxyphene napsylate in 161 patients, ages 18-55 yr, with severe postoperative pain after cesarean section. The 3 active treatments were effective analgesics, statistically superior to placebo. The 150 mg **tramadol** hydrochloride dose provided significantly greater analgesia over the lower dose. The 75 mg dose of **tramadol** hydrochloride was generally more effective than the acetaminophen-**propoxyphene** napsylate combination after hour 2, and significantly so for some hourly time points. The 150 mg dose of **tramadol** was significantly more effective than the acetaminophen-**propoxyphene** napsylate combination from hour 2 through hour 6. No serious adverse effects were observed; however, dizziness was more frequently reported with the 150 mg dose. It was concluded that **tramadol** hydrochloride at both dose levels is an effective analgesic agent.
M. Therese Gyi

L6 ANSWER 1 OF 20 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2000:235461 BIOSIS
DN PREV200000235461
TI A drug use evaluation of selected opioid and nonopioid analgesics in the nursing facility setting.
AU Cramer, Gena W.; Galer, Bradley S.; Mendelson, Marilyn A.; Thompson, Gregory D. [Reprint author]
CS Medical Affairs, Center for Health Information, 3101 American Legion Road, Suite 21, Chesapeake, VA, 23321, USA
SO Journal of the American Geriatrics Society, (**April, 2000**) Vol. 48, No. 4, pp. 398-404. print.
CODEN: JAGSAF. ISSN: 0002-8614.
DT Article
LA English
ED Entered STN: 7 Jun 2000
Last Updated on STN: 5 Jan 2002

L6 ANSWER 2 OF 20 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 1998:438656 BIOSIS
DN PREV199800438656
TI Non-NSAID pharmacologic treatment options for the management of chronic pain.
AU Schnitzer, Thomas J. [Reprint author]
CS Office Clinical Res. Training, Northwestern Univ., Abbott Hall, 5th Floor, 710 N. Lakeshore Drive, Chicago, IL 60611, USA
SO American Journal of Medicine, (**July 27, 1998**) Vol. 105, No. 1 PART B, pp. 45S-52S. print.
CODEN: AJMEAZ. ISSN: 0002-9343.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 7 Oct 1998
Last Updated on STN: 7 Oct 1998

L6 ANSWER 3 OF 20 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 1997:170766 BIOSIS
DN PREV199799477369
TI Single-patient data meta-analysis of 3453 postoperative patients: Oral tramadol versus placebo, codeine and combination analgesics.
AU Moore, R. A. [Reprint author]; McQuay, H. J.
CS Pain Res. Nuffield Dep. Anaesthetics, Univ. Oxford, Oxford Radcliffe Hosp., The Churchill, Headington, Oxford OX3 7LJ, UK
SO Pain, (**1997**) Vol. 69, No. 3, pp. 287-294.
CODEN: PAINDB. ISSN: 0304-3959.
DT Article
LA English
ED Entered STN: 24 Apr 1997
Last Updated on STN: 24 Apr 1997

L6 ANSWER 4 OF 20 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 1997:70436 BIOSIS
DN PREV199799369639
TI A novel approach to the pharmacology of analgesics.
AU Raffa, Robert B.
CS Temple Univ. Sch. Pharmacy, 3307 N. Broad St., Philadelphia, PA 19140, USA
SO American Journal of Medicine, (**1996**) Vol. 101, No. 1 PART A, pp.

40S-46S.
CODEN: AJMEAZ. ISSN: 0002-9343.
DT Article
LA English
ED Entered STN: 11 Feb 1997
Last Updated on STN: 11 Feb 1997

L6 ANSWER 5 OF 20 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 1995:498900 BIOSIS
DN PREV199598522450
TI Serotonin and norepinephrine uptake inhibiting activity of centrally acting analgesics: Structural determinants and role in antinociception.
AU Codd, Ellen E. [Reprint author]; Shank, Richard P.; Schupsky, James J.; Raffa, Robert B.
CS R.W. Johnson Pharmaceutical Research Inst., Welsh and McKean Roads, Spring House, PA 19477-0776, USA
SO Journal of Pharmacology and Experimental Therapeutics, (**1995**) Vol. 274, No. 3, pp. 1263-1270.
CODEN: JPETAB. ISSN: 0022-3565.
DT Article
LA English
ED Entered STN: 29 Nov 1995
Last Updated on STN: 27 Jan 1996

L6 ANSWER 6 OF 20 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 1992:394171 BIOSIS
DN PREV199294066346; BA94:66346
TI ANALGESIC ORAL EFFICACY OF TRAMADOL HYDROCHLORIDE IN POSTOPERATIVE PAIN.
AU SUNSHINE A [Reprint author]; OLSON N Z; ZIGHELBOIM I; DECASTRO A; MINN F L
CS ANALGESIC DEV LTD, 907 FIFTH AVE, SUITE 1 EAST, NEW YORK, NY 10021, USA
SO Clinical Pharmacology and Therapeutics, (**1992**) Vol. 51, No. 6, pp. 740-748.
CODEN: CLPTAT. ISSN: 0009-9236.
DT Article
FS BA
LA ENGLISH
ED Entered STN: 24 Aug 1992
Last Updated on STN: 1 Oct 1992

L6 ANSWER 7 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:337094 CAPLUS
DN 126:313264
TI Tramadol distribution in four postmortem cases
AU Levine, Barry; Ramcharitar, Vera; Smialek, John E.
CS Office of the Chief Medical Examiner, Baltimore, MD, 21201, USA
SO Forensic Science International (**1997**), 86(1,2), 43-48
CODEN: FSINDR; ISSN: 0379-0738
PB Elsevier
DT Journal
LA English

L6 ANSWER 8 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:578300 CAPLUS
DN 125:264647
TI A novel approach to the pharmacology of analgesics
AU Raffa, Robert B.
CS RW Johnson Pharmaceutical Research Institute, Spring House, PA, 19140, USA
SO American Journal of Medicine (**1996**), 101(1A), 40S-46S
CODEN: AJMEAZ; ISSN: 0002-9343
PB Excerpta Medica

DT Journal; General Review
LA English

L6 ANSWER 9 OF 20 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:548897 CAPLUS
DN 121:148897
TI Withdrawal characteristics following frequent intravenous administration of several opioids in rats
AU Wakasa, Yoshio; Kawaguchi, Takeshi; Yanagita, Tomoji
CS Preclin. Res. Div., Cent. Inst. Exp. Anim., Kawasaki, 216, Japan
SO Arukoru Kenkyu to Yakubutsu Izon (**1994**), 29(1), 40-51
CODEN: AKYIDF; ISSN: 0389-4118
DT Journal
LA Japanese

L6 ANSWER 10 OF 20 EMBASE
on STN
AN 2003331505 EMBASE
TI Pain management in a long-term care facility: Compliance with JCAHO standards.
AU Mullins C.R.; Wild T.L.
CS C.R. Mullins, Baptist Hospital of Cocke County, Newport, TN 37871, United States. rmullins@planetc.com
SO Journal of Pain and Palliative Care Pharmacotherapy, (**2003**) 17/2 (63-70).
Refs: 8
ISSN: 1536-0288 CODEN: JPPCBG
CY United States
DT Journal; Article
FS 008 Neurology and Neurosurgery
017 Public Health, Social Medicine and Epidemiology
037 Drug Literature Index
LA English
SL English

L6 ANSWER 11 OF 20 EMBASE
on STN
AN 1999223129 EMBASE
TI [Therapy with opioids in liver or renal failure].
EINSATZ VON OPIOIDEN BEI LEBER- ODER NIERENINSUFFIZIENZ.
AU Tegeder I.; Geisslinger G.; Lotsch J.
CS Dr. I. Tegeder, Zentrum der Pharmakologie, Klinikum, J.-Wolfgang-Goethe-Univ. Frankfurt, Theodor Stern Kai 7, D-60590 Frankfurt am Main, Germany
SO Schmerz, (**1999**) 13/3 (183-195).
Refs: 1
ISSN: 0932-433X CODEN: SCMZA
CY Germany
DT Journal; General Review
FS 008 Neurology and Neurosurgery
028 Urology and Nephrology
037 Drug Literature Index
LA German
SL English; German

L6 ANSWER 12 OF 20 EMBASE
on STN
AN 1999091804 EMBASE
TI Opioid drug-drug interactions: A review.
AU Liston H.L.; Markowitz J.S.
CS J.S. Markowitz, Institute of Psychiatry, Medical University of South Carolina, 850 MUSC Complex, Charleston, SC 29425, United States
SO Journal of Pharmacy Practice, (**1998**) 11/5 (325-341).

Refs: 88
ISSN: 0897-1900 CODEN: JPPREU
CY United States
DT Journal; General Review
FS 030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English

L6 ANSWER 13 OF 20 TOXCENTER COPYRIGHT 2004 ACS on STN
AN 2003:261507 TOXCENTER
CP Copyright 2004 ASHP
DN 40-18479
TI The toxicology of substance abuse: opiates and opioids
AU Kearney, TE
SO ASHP Midyear Clinical Meeting, (**DEC 2003**) Vol. 38, pp. PI-117.
DT Abstract
FS IPA
OS IPA 2003:18470
LA English
ED Entered STN: 20031104
Last Updated on STN: 20031104

L6 ANSWER 14 OF 20 TOXCENTER COPYRIGHT 2004 ACS on STN
AN 2002:199605 TOXCENTER
CP Copyright 2004 ASHP
DN 39-10936
TI Highlights of the 22nd French pharmacovigilance meeting
AU Anonymous
SO Prescrire International (France), (**2002**) Vol. 11, pp. 21-23. 27 Refs.
CODEN: PRINFU. ISSN: 1167-7422.
DT General Review
FS IPA
OS IPA 2002:10935
LA English
ED Entered STN: 20020917
Last Updated on STN: 20020917

L6 ANSWER 15 OF 20 TOXCENTER COPYRIGHT 2004 ACS on STN
AN 2002:85239 TOXCENTER
CP Copyright 2004 ASHP
DN 38-04248
TI Hear my song: auditory hallucinations with tramadol hydrochloride
AU Keeley, P. W.; Foster, G.; Whitelaw, L.
CS Strathcarron Hospice, Denny, Stirlingshire FK6 5HJ, England Internet: Paulkeeley@hotmail.com
SO British Medical Journal (England), (**Dec 23-30 2000**) Vol. 321, p. 1608. 7 Refs.
CODEN: BMJOAE. ISSN: 0959-8146.
DT Journal
FS IPA
OS IPA 2002:4363
LA English
ED Entered STN: 20020416
Last Updated on STN: 20020416

L6 ANSWER 16 OF 20 TOXCENTER COPYRIGHT 2004 ACS on STN
AN 2001:69960 TOXCENTER
CP Copyright 2004 ACS
DN CA13510133217D

TI Epidemiological survey on poly-drug abuse among drug addicts
AU Liu, Zhi-Min; Zhou, Wei-Hua; Lian, Zhi; Mu, Yue; Cao, Jia-Qi; Cai, Zhi-Ji; Yang, Zheng; Song, Sen-Lin; Gong, Wen-Lin; et al.
CS National Institute Drug Dependence, Beijing Medical Univ., 100083, Peop. Rep. China.
SO Zhongguo Linchuang Yaolixue Zazhi, (**2000**) Vol. 16, No. 4, pp. 272-276.
CODEN: ZLYZE9. ISSN: 1001-6821.
CY CHINA
DT Journal
FS CAPLUS
OS CAPLUS 2001:19345
LA Chinese
ED Entered STN: 20011116
Last Updated on STN: 20020319

L6 ANSWER 17 OF 20 TOXCENTER COPYRIGHT 2004 ACS on STN
AN 2000:2827 TOXCENTER
CP Copyright 2004 ASHP
DN 37-12040
TI Use of opioids for chronic nonmalignant pain
AU Chernin, T.
SO Pharmacy Times (USA), (**Dec 1999**) Vol. 65, pp. 18-20, 23-25. 17 Refs.
CODEN: PYTMAO. ISSN: 0003-0627.
DT Journal
FS IPA
OS IPA 2000:12039
LA English
ED Entered STN: 20011116
Last Updated on STN: 20011116

L6 ANSWER 18 OF 20 TOXCENTER COPYRIGHT 2004 ACS on STN
AN 1998:66091 TOXCENTER
DN PubMed ID: 10183392
TI Tramadol: new preparation. Capsules: central analgesic; step 2 on the WHO scale
AU Anonymous
SO Prescrire international, (**1998 Feb**) 7 (33) 9-12.
Journal Code: 9439295. ISSN: 1167-7422.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
FS MEDLINE
OS MEDLINE 1998620199
LA English
ED Entered STN: 20011116
Last Updated on STN: 20011116

L6 ANSWER 19 OF 20 TOXCENTER COPYRIGHT 2004 ACS on STN
AN 1994:3496 TOXCENTER
CP Copyright 2004 ASHP
DN 32-12018
TI Tramadol versus dextropropoxyphene in the treatment of osteoarthritis: short term double-blind study
AU Jensen, E. M.; Ginsberg, F.
CS Dept. of Rheumatol., Bispebjerg Hosp., Bispebjerg Bakke 23, Dk-2400 Copenhagen, Denmark
SO Drug Investigation (New Zealand), (**Oct 1994**) Vol. 8, pp. 211-218. 27 Refs.
CODEN: DRUIEA. ISSN: 0114-2402.
DT Journal
FS IPA

OS IPA 94:13260
LA English
ED Entered STN: 20011116
Last Updated on STN: 20011116

L6 ANSWER 20 OF 20 TOXCENTER COPYRIGHT 2004 ACS on STN
AN 1992:1697 TOXCENTER
CP Copyright 2004 ASHP
DN 30-01737
TI Analgesic oral efficacy of tramadol hydrochloride in postoperative pain
AU Sunshine, A.; Olson, N. Z.; Zighelboim, I.; DeCastro, A.; Minn, F. L.
CS New York Univ. Med. Ctr., New York, NY, USA Reprints: Analgesic Dev. Ltd., 907 Fifth Ave., Suite 1 E., New York, NY 10021, USA
SO Clinical Pharmacology and Therapeutics (USA), (**Jun 1992**) Vol. 51, pp. 740-746. 14 Refs.
CODEN: CLPTAT. ISSN: 0009-9236.
DT Journal
FS IPA
OS IPA 92:6398
LA English
ED Entered STN: 20011116
Last Updated on STN: 20011116